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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	PAPER NUMBER
1646	10

DATE MAILED: 07/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/993,344	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 39-46* is/are pending in the application.

4a) Of the above claim(s) *39-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the claims

1. Claim 1 has been amended, claims 2-38 have been cancelled and claims 39-46 have been added as requested in the amendment of Paper No. 11, filed on June, 09, 2003. Claims 1 and 39-46 are pending in the instant application.

Election/Restrictions

2. Applicant's election with traverse of Group I in Paper No. 11 is acknowledged. The traversal is on the ground(s) that SEQ ID NOS: 1 and 3 are fragments of apolipoprotein J precursor protein and SEQ ID NO: 1 and 2 share some structural similarities, they are identified as markers predictive of Alzheimer's disease, thus, they share a common utility and common structural feature and, therefore, claims 1, 18, 29, 30, 33, 34 and 38 are proper Markush claims. These arguments have been found to be persuasive in part. The Examiner acknowledges that because polypeptides of SEQ ID NO: 1, 2 and 3 are asserted to be indicative of Alzheimer's disease and, therefore, share a common utility, the objections to the claims 1, 18, 29, 30, 33, 34 and 38 as being improper Markush claims is withdrawn. However, because each of the recited sequences represents a non-overlapping fragment of a larger sequence and each fragment could be embedded within other patentably distinct proteins, a separate search is required for each possible fragment, the restriction is still deemed proper. Applicant's argument regarding examination of "three short amino acid sequences, seven sequences less than the ten sequences normally considered by the Office as reasonable for examination purposes" (bottom at page 7 of the Response) has been fully considered but is not deemed to be persuasive for the following

reasons. MPEP 804.03 is directed to nucleotide sequences, in which the Commissioner authorized a partial waiver of restriction practice, allowing the examination of up to ten sequences. This waiver was issued in 1996. Since then, the nucleic acid and protein databases that must be searched for each of the independent and distinct sequences claimed herein have multiplied many fold in size, such that it is now burdensome to search more than a single sequence in an application. Further, the waiver allowed, but did not require the Examiner to search up to ten sequences. Also, the waiver was directed to nucleotide sequences and not amino acids sequences, which is the case in the instant application.

The requirement is still deemed proper and is therefore made FINAL.

Newly submitted claims 39-46 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 39-43 are drawn to a method for diagnosing Alzheimer's disease and claims 44-46 are drawn to a diagnostic kit. Inventions of claims 39-46 and claims 44 –46 and the elected invention of Group I (claim 1) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the peptide of claim 1 could be used in an entirely different manner such as for the production of antibodies rather than in the methods of claims 39-43 or in a kit with an antibody of claims 44-46.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution

on the merits. Accordingly, claims 39-46 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. Applicant's reference to the decision in *In re Ochiai*, 71 F.3d 1565, (page 8, last paragraph) is noted but is not deemed persuasive, as PTO practice in view of that decision is directed to rejoinder of claims after allowable subject matter has been indicated, and not to withdrawal of restriction requirements. Applicant is advised that at such time as elected product claim(s) are indicated as being allowable, rejoinder of claims drawn to methods of using such may be requested under 35 U.S.C. § 103(b) pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86). Such rejoinder is *not* tantamount to a withdrawal of the restriction requirement.

Claim 1 is under examination in the instant office action.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claim 1 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claim fails to include any limitations, which would distinguish the claimed polypeptide sequences from those which occur in nature. In the absence of the hand of man, naturally occurring nucleic acid molecules and proteins are considered non-statutory subject matter. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Additionally, mere purity of a

naturally occurring product does not necessarily impart patentability. Ex parte Siddiqui, 156 USPQ 426 (1966). However, when purity results in a new utility, patentability is considered. Merck Co. v. Chase Chemical Co., 273 F. Supp. 68 (1967). Filing of evidence of a new utility imparted by the increased purity of the claimed invention and amendment of the claims to recite a purity limitation, if supported by the specification, is suggested to obviate this rejection. Applicant should point to the basis in the specification for any amendment to the claims.

5. Claim 1 is further rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of a peptide. The instant application does not disclose a specific biological role for this peptide, or its significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect.

Claim 1 is drawn to a biopolymer marker peptide consisting of amino acid residues 2-18 of SEQ ID NO: 1 useful in diagnosis of Alzheimer's disease. However, the instant specification fails to provide any information on how to use the disclosed peptide 2-18 of SEQ ID NO: 1 as a marker of Alzheimer's disease. There is no information disclosed in the instant specification, which would provide evidence or sound scientific reasoning that a biopolymer marker, which is a fragment 2-18 of SEQ ID NO: 1, is specifically associated with Alzheimer's disease.

The nature of the invention is the finding of specific fragments of apolipoprotein J precursor protein, which are fragments 2-18 of SEQ ID NO: 1 and 2-13 of SEQ ID NO: 3, and also a fragment of sulfated glycoprotein-2, which is SEQ ID NO: 2, residues 2-18, and which are asserted to be associated with Alzheimer's disease, in a serum sample treated according to a protocol provided on pages 40-46 of the instant specification. The state of the art is such that it

does not recognize any specific association of the fragment 2-18 of a peptide of SEQ ID NO: 1 with Alzheimer's disease. Therefore, in the absence of information in the prior art, one skilled in the art would have to solely depend on the instant disclosure to practice the claimed invention. Accordingly, the instant invention, as claimed, allows the detection of a peptide consisting of the amino acid sequence 2-18 of SEQ ID NO: 1 in any sample in general to lead to diagnosis of Alzheimer's disease. However, the instant specification fails to provide any guidance on how the detection of a biopolymer marker peptide 2-18 of SEQ ID NO: 1 in any sample can be used in diagnosis of Alzheimer's disease.

Furthermore, it is stated on page 46, last paragraph of the instant specification that "Figures 1, 3 and 5 are photographs of a gel which is indicative of the presence/absence of the marker in disease vs. control and, in cases where the marker is always present, the relative strength, e.g. the up or down regulation of the marker relative to categorization of disease state is deduced". Based on the limited information on how to conduct mass spectrometric analysis of a sample presented in the instant specification and on the analysis of the Figures, one skilled in the art clearly would not be able to use the peptide 2-18 of SEQ ID NO: 1 as a biopolymer marker for Alzheimer's disease. First, the instant specification fails to explain what is the relationship between a peptide 2-18 of SEQ ID NO: 1 and "particular disease state". While it is not necessary that Applicant understands or discloses the mechanism by which the invention functions, in this case, in the absence of such an understanding the following questions must be answered. Is it "the up or down regulation of the marker relative to categorization of disease state"? Or is "the presence/absence" of the peptide 2-18 of SEQ ID NO: 1 indicative of a disease?

Also, it is well known in the art that a diagnosis of Alzheimer's disease is only definitive at postmortem examination or at brain biopsy (see Clark et al., 1993, and Motter et al, 1995, for example). The instant specification, as originally filed, fails to disclose any specific information regarding the data presented in Figures 1-6, such as, for example, description of a sample, the representative number of samples, description of control samples, and, most importantly, a method of evaluation that the "Band AD-H-S-D3(E)C2" on Figure 1 or "Band 1A Inconclusive" and "Band 2A Inconclusive" are indicative of Alzheimer's disease. The text on page 11, third paragraph, states that "a biopolymer marker which is strongly present in a normal individual, but is down-regulated in disease is predictive of said disease; while alternatively, a biopolymer marker which is strongly present in a disease state, but is down-regulated in normal individuals, is indicative of said disease state".

Thus, Applicant's invention is predicated on the finding that a serum sample being processed according to the disclosed protocol contains a peptide 2-18 of SEQ ID NO: 1. Applicant further extrapolates this result into an assertion that SEQ ID NO: 1 can be used as a biopolymer marker for Alzheimer's disease. Accordingly, it would appear that Applicant provides a single finding (the finding), and then presents an invitation to experiment to determine if a peptide 2-18 of SEQ ID NO: 1 is predictive of Alzheimer's disease. Such experimentation would include determination if a marker 2-18 of SEQ ID NO: 1 is absent or present or strongly present in a person suspected having Alzheimer's disease *versus* normal individual, or is up- or down-regulated in disease.

The Declaration of Lander under 37 CFR 1.132 filed on June 06, 2003, Paper No. 10 is insufficient to overcome the rejection of claim 1 because it presents additional information that

the instant claimed peptide is not in normal human serum, such diagnostic relationship does not appear to be taught by the instant specification, as originally filed. 35 USC § 101 clearly states that the invention must be useful in currently available form, which precludes any further experimentation to establish the utility of the claimed invention. The fact that Applicant submits additional data resulted from further experimentation to support the claimed invention, confirms that the instant invention was not completed as filed, and, therefore, clearly lacks utility in currently available form.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which the court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

Thus, to employ a peptide of the instant invention as a marker for Alzheime'rs disease would clearly be using it as the object of further research, which has been determined by the courts to be a utility, which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for the clamed peptide in their currently available

form, then the instant invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 1 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 1 is vague and ambiguous because it is not clear what limitation the recitation "diagnostic for Alzheimer's disease" adds to the claimed subject matter.

Conclusion

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.
July 17, 2003

JOHN ULM
PRIMARY EXAMINER
GROUP 1600